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RANOLAZINE FOR THE TREATMENT OF DIASTOLIC HEART FAILURE IN PATIENTS WITH PRESERVED EJECTION FRACTION: RESULTS FROM THE RALI-DHF STUDY

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Background: Heart failure with preserved ejection fraction (HFpEF) accounts for 50% of all HF patients. Currently, there is no specific treatment for diastolic dysfunction. Ranolazine may improve diastolic function by inhibiting the late Na current. We investigated if ranolazine improved diastolic function in patients with HFpEF.

Methods: RALI-DHF was a prospective, single-center, randomized, double-blind, placebo-controlled exploratory study. Inclusion criteria were: EF≥45%, E/E'>15 or NT-proBNP>220 pg/mL, LVEDP≥18 mmHg, and time-constant of relaxation, tau ≥50 ms. Patients were randomized to receive i.v. infusion of ranolazine (n=12) or placebo (n=8) during catheterization and for 24 h, followed by oral treatment with ranolazine 1000 mg twice daily or placebo for 14 days.

Results: After 30 min of infusion LVEDP decreased significantly in the ranolazine group (from 21.3 to 19.1 mmHg, p=0.04) but not in the placebo group. PCWP also decreased in the ranolazine group (p=0.04) and was significantly different from placebo (p=0.05). Mean PAP showed a trend towards a decrease in the ranolazine group (from 24.4 to 22.2 mmHg, p=0.08) that was significant under pacing conditions (from 26.5 to 25.2, p=0.02) but not for placebo. These changes occurred without decreases in LVESP, systemic or pulmonary resistance in the ranolazine group. There were no changes with respect to relaxation kinetics (e.g. tau, dP/dTmin). During cardiopulmonary exercise test (CPET) repeated after 14 days of treatment, the exercise ventilation/carbon dioxide production ratio (VE/VCO2 slope), an index of ventilatory response to exercise and strong predictor of mortality in patients with HF, showed a numerically decrease in the ranolazine group (from 34.2 to 30.5), and no change (33.6 and 34.4) in the placebo group (p=ns; ranolazine vs placebo). Exercise duration increased numerically by a mean of 55 and 38 s in the ranolazine and placebo groups, respectively. There were no effects on echocardiographic parameters or NT-pro-BNP.

Conclusions: The results of this exploratory, proof-of-concept study revealed improvement with ranolazine in some important measures of diastolic function.